PATHOLOGY

RR-8.0

Contents

HEMATOLOGY : INTRODUCTION TO WBC DISORDERS AND LEUKEMIAS

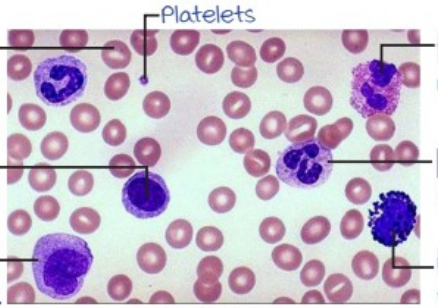
----- Active space -----

Introduction to Hematology

00:01:35

PERIPHERAL SMEAR (PS)

Only mature cells ⊕



RBC : Central 1/3rd pallor.

Lymphocyte (Smallest) : Round nucleus, no granules.

Monocyte (Largest) : Reniform/kidney-shaped nucleus.

Eosinophil : Bilobed nucleus, brick red granules.

Neutrophil : 3-5 lobes in nucleus, bluish granules.

Basophil : Dense purple granules obscuring cytoplasm.

Normal PS

Types of WBCs :

1. Agranulocytes : No granules in cytoplasm.
2. Granulocytes : Granules ⊕ in cytoplasm.

BONE MARROW EXAMINATION

Position : Ⓛ Lateral, back facing the doctor

Sites :

- Adults : Iliac crest (PSIS > ASIS) > Sternum.
- Children : Tibia (Shin).

Types of needles :

- Salah's.
- Klima.
- Jamshidi : Can be used for BM biopsy & aspiration.

Salah's needle

Bone Marrow Aspirate (BMA) :

Dry tap : Dry needle on attempted BMA → Needs BM bx.

Causes :

- Aplastic anemia : Fat > Cells.
- Myelofibrosis.
- Hairy cell leukemia.
- AML-M7 : ↑Platelet derived growth factor → Myelofibrosis.
- Space occupying lesions in BM : Granuloma, metastasis.

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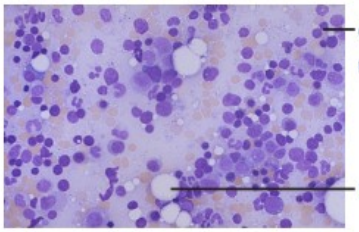
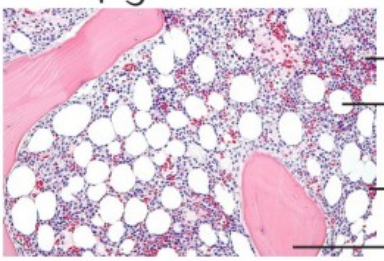
Appearance : Both mature & immature cells (+)



Normal myeloid : erythroid (M:E) ratio → 3:1 to 15:1

BMA

Bone Marrow Biopsy (BM bx) :



BM bx

WBC Disorders

00:15:35

(N) TLC : 4000–11,000/mm^3.

Infection : > 11,000/mm^3.

Non-Neoplastic Disorders :

Neutrophilia (> 40–70%) :

- Acute/bacterial infections.
- Tissue necrosis : Burns, MI.

Monocytosis (> 1–8%) :

- Chronic infections : TB.
- Rickettsia.
- IBD.
- Malaria.

Eosinophilia (> 2–6%) :

- Allergic reactions : Asthma, hay fever, Type I hypersensitivity.
- Parasitic infections.
- Malignancy : Hodgkin's lymphoma.
- Tropical pulmonary eosinophilia.

Basophilia (≥ 1%) : myeloproliferative disorders (CML).

Lymphocytosis (> 15–40%) : Chronic/Viral infections.

Note :

1. Tuberculosis : Bacterial infection with lymphocytosis.
2. Splenomegaly + ↓Neutrophil alkaline phosphatase (NAP) score + Basophilia → myeloproliferative disorder (CML)

Morphological Abnormalities :

1. Abnormal number of lobes in the nucleus :

	Hypersegmented neutrophil	Hyposegmented neutrophil/Pseudo-Pelger-Huet cell
No. of lobes	> 5 lobes	< 3 lobes
Seen in	Megaloblastic anemia d/t : Vit B12 deficiency	Myelodysplastic syndrome

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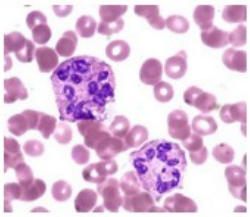
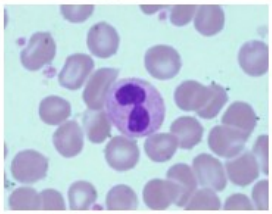
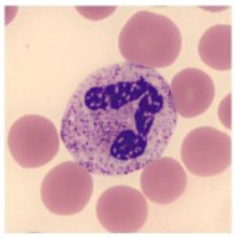
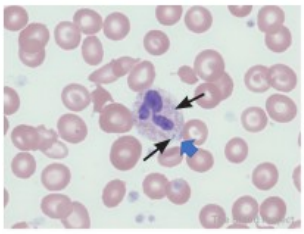
	Hypersegmented neutrophil	Hyposegmented neutrophil/Pseudo-Pelger-Huet cell
Appearance on PS		

2. Abnormalities d/t infection :



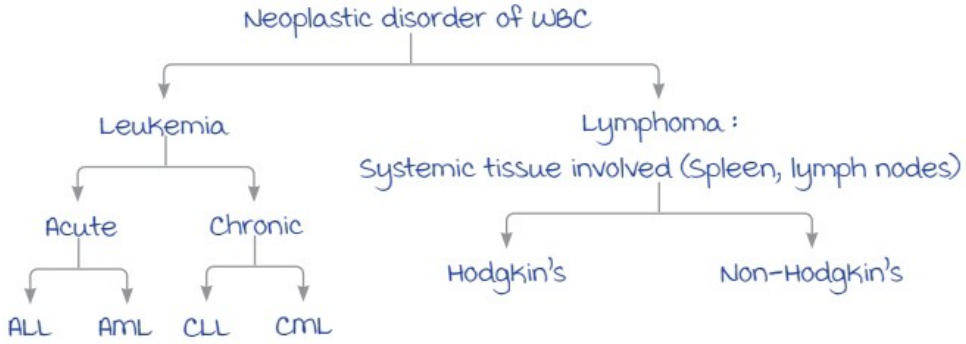
Toxic granules



Dohle bodies :

Patches of dilated endoplasmic reticulum.

Neoplastic Disorders :



Acute Leukemias

00:27:42

Diagnostic criteria :

WHO :

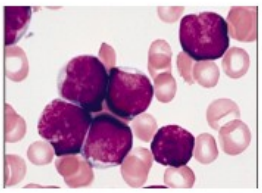
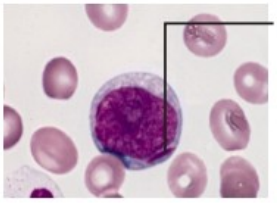
- > 20% blasts (Immature precursors) in BM/PS OR
- < 20% blasts + t(15:17)/t(8:21)/Inversion-16 translocation.

FAB : > 30% blasts in BM/PS.

Types of blasts :

	Lymphoblast	Myeloblast
Size	Small	Large
Cytoplasm	Scanty	Moderate amount
Granules	Absent	Present
Auer rods	Absent	Present (Clusters → Faggot cells)
Chromatin	Coarse, dark blue, clumped	Homogenous, opened up, pink

----- Active space -----

	Lymphoblast	Myeloblast
Nucleoli	Inconspicuous	2–5, prominent
Special stain	PAS	Myeloperoxidase (MPO), Sudan black B (SBB), Non specific esterase (NSE)
Appearance		
↑(> 20%) in	ALL	AML

ALL

00:35:54

Age at presentation : 2–9 yrs (m/c leukemia in children).

Clinical features :

- D/t ↑blasts → ↓mature cells → Hepatosplenomegaly
  - ↓RBC → Pallor, fatigue.
  - ↓WBC → ↑Infections.
  - ↓Platelets → Bleeding manifestation.
- Involvement of CNS, testes & LN (Absent in AML).

Classification :

FAB classification (Based on morphology) :

		L1	L2	L3
Morphology	Blast	 Small, round	 Pleomorphic, larger	 Large
	Cytoplasm	Scant	Moderate	Moderate, basophilic, vacuolated
	Nucleus	Round	Irregular	Round/oval
	Chromatin	Homogenous	Fine	Stippled
	Nucleoli	Indistinct	≥ 1, large, distinct	
Occurrence		75% (m/c)	20 %	5 %
Prognosis		Best	-	Worst

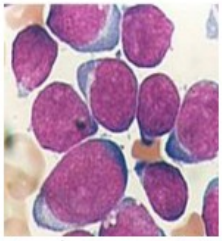
WHO classification (Based on flowcytometric markers) :

	B-ALL	T-ALL
Occurrence	85 % (m/c)	10-15 % (L/c)
Age group affected	Usually children	Usually adults & adolescent
Mediastinal involvement	Absent	Present
Associated mutation	LOF in PAX5, E2A, RUNX1, EBF gene	GOF in NOTCH-1 gene
Prognosis	Better	Poor

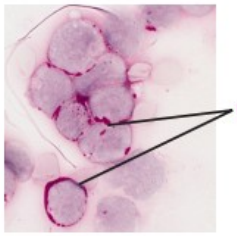
----- Active space -----

Investigations :

1. CBC :
   - ↓Hb, Platelets.
   - ↑/↓ WBC's.
2. PS :
   - > 20% lymphoblasts.
   - Special stain : PAS (Block/Dot) +ve.
3. Flowcytometric markers :
   - B-ALL : CD19, CD20, CD22, PAX5, TdT, CALLA.
   - T-ALL : CD1, CD2, CD3, CD5, CD7, TdT, CALLA.



Hand mirror cells in ALL



PAS staining

Note :

AML-M6 : PAS (Diffuse) +ve.

Prognostic Factor :

	Good prognosis	Bad Prognosis
Age	2-9	<1, >10
Sex	F	m
Race	Whites	Blacks
FAB type	L1	L2, L3
WHO type	B-ALL	T-ALL
Organ involvement		
CNS	⊖	⊕
Testis	⊖	⊕
Lymph node	⊖	⊕
Cytogenetics	Hyperdiploidy Trisomy 4, 7, 10, t(12;21)	Hypodiploidy t(9;22)
Leucocyte count	<1, 00, 000/mL	>1, 00, 000/mL

Note : If t(9;22) present in CML → Good prognosis.

Treatment :

VAPD regimen
- Vincristine.
- L-Asparaginase.
- Prednisolone.
- Doxorubicin.

----- Active space -----

AML

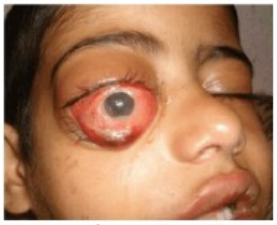
00:47:55

Age at presentation : 15-39 yrs (Same as CML).

Clinical features : Similar to ALL.

Additionally :

- Gum hypertrophy/bleeding.
- DIC.
- Chloroma : Soft tissue involvement.
  - MPO +ve.
  - M/c site : Orbit.
  - Arbiskov cells : Monocytes in chloroma.



Chloroma/Granulocytic sarcoma

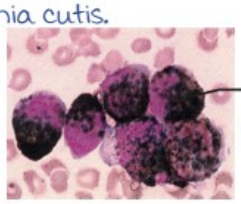
Classification :

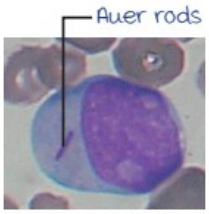
FAB classification :

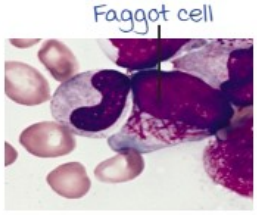
	Cell type + Degree of differentiation	Special Features
M0	Undifferentiated AML	-
M1	AML with minimum maturation	-
M2 (M/C)	AML with maturation	A/W : t(8;21) & chloroma
M3	Acute promyelocytic leukemia	• Best prognosis. • Maximum Auer rods (+) ⟶ Faggot cells (+) • A/W : - t(15;17) ⟶ Run X_1/RunX_1T_1 - DIC • Rx : All-trans retinoic acid, Arsenic trioxide.
M4	Acute myelomonocytic leukemia	Inversion 16
M4 eos	Acute myelomonocytic leukemia with eosinophilia	-
M5	Monocytic leukemia (a & b variants)	-
M6	Acute erythroid leukemia	• AKA Di Guglielmo disease. • Diffusely PAS +ve
M7 (L/C)	Acute megakaryocytic leukemia	• A/W : - Down's syndrome - Myelofibrosis ⟶ Dry tap on BMA. • Markers : CD41, CD61

Common features of M4, M5 :

- M/c a/w gum bleeding (M5 > M4).
- NSE +ve (D/t monoblasts).
- Leukemia cutis.







Myeloblasts

CML

01:00:17 ----- Active space -----

Age at presentation : Middle age to elderly.

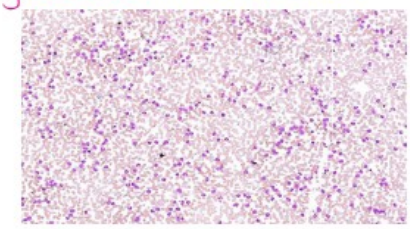
Pathogenesis :

t(9;22) ⟶ Philadelphia chromosome ⟶ Constant activation of tyrosine kinase (TK) ⟶ Myeloproliferation.
(In 95% cases)

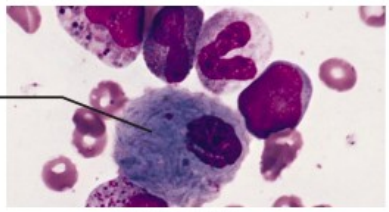
Clinical features : Massive splenomegaly ⟶ Dragging sensation in the abdomen.

Investigations :

1. CBC : Ⓝ Hb, ↑↑WBC, ↑↑Platelets.
2. PS : Looks like BM.
   - Basophilia.
   - All stages of myeloid maturation ⊕.
3. BMA :
   - Sea blue histiocyte.
   - Pseudo Gaucher cell
4. NAP score : ↓ (Ⓝ ⟶ 40-100).
5. Fluorescent in situ hybridization (FISH) : t(9;22).



PS in CML

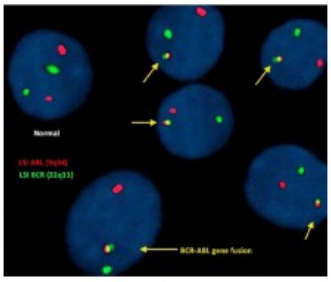


BMA in CML

Treatment : Imatinib mesylate (Inhibits TK).

WHO criteria for CML in accelerated phase :

- Blasts 10-19% in blood and/or bone marrow.
- Peripheral blood basophils > 20%.
- Persistent thrombocytopenia (< 100 x 10^9/L) unrelated to therapy, (or) thrombocytosis (>1000 x10^9/L) unresponsive to therapy.
- Increasing spleen size and increasing WBC unresponsive to therapy.
- Cytogenetic evidence of clonal evolution.



FISH analysis in CML

Note :

1. D/D for massive splenomegaly :
   - Malaria
   - Kala azar
   - Polycythemia vera.
   - MDS (CML).
   - Myelofibrosis.
   - Gaucher's disease.
2. NAP score :

- ↓ ⟶ Paroxysmal Nocturnal Hemoglobinuria (PNH), CML.
- ↑ ⟶ Leukemoid reaction, pregnancy, stress, other myeloproliferative disorders.

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CLL

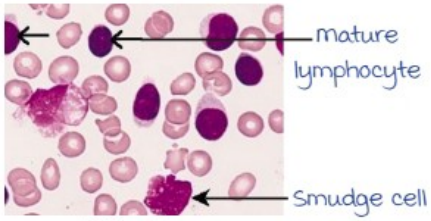
01:09:07

Age at presentation : Elderly (60-70yrs).

Pathogenesis : Deletion of 13q, 11q, 17p; Trisomy 12.

Clinical features :

- Painless lymphadenopathy.
- H/o Autoimmune Hemolytic Anemia (AIHA).



PS in CLL

Investigations :

1. CBC : Absolute lymphocytosis (> 5000/mm^3).
2. PS :
   - Mature lymphocytosis.
   - ↑Smudge/Parachute/Basket cells.
3. Lymph node bx : Proliferation centers (Pathognomonic).
4. Markers : CD5, CD23, CD200.

Note :

- CLL : Convent girl appearance (Uniform appearance of cells).
- CML : College girl appearance (No cell uniformity).

Summary of Leukemia

01:12:20

	ALL	AML	CLL/SLL	CML
Age	2-9 yrs	15-39 yrs	6th or 7th decade	Elderly
Special C/f	• CNS • Testis • Lymph node involvement	• Gum bleeding • Chloroma • DIC	• AIHA • Lymphadenopathy	Massive splenomegaly
P/S	> 20% lymphoblasts	> 20% myeloblasts	↑Lymphocyte count, Smudge cells.	All stages of myeloid maturation, basophilia.
Stain	PAS ⊕	MPO, Sudan black B, Oil red O	-	-
markers	B ALL : CD 19, 10 ; PAX 5, T ALL : CD 1, 2, 5, 7 Both : TdT ⊕	CD 13, 33, 117 MPO	CD 5+, CD23+, CD200+	-
Cytogenetics	-	t(8;21) ⟶ M2 t(15;17) ⟶ M3 inv(16) ⟶ M4	Trisomy 12 del 13q, 17p	t(9;22)